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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Int'l Appln No.:	PCT/IL00/00046	§
Int'l Filing Date:	24 January 2000	§
Priority Date Claimed:	03 February 1999	§
Title:	TRANSGENIC PLANTS	§
Applicant:	YEDA RESEARCH AND DEVELOPMENT CO. LTD.	§
Attorney Docket:	00/20550 (Previously 34/52)	§

RESPONSE

BOX PCT
Commissioner of Patents and Trademarks
Washington, D.C. 20231

Dear Sir:

This is a response to a Written opinion sent March 6, 2001, a response to which is due, and being made, within one month.

Claim 2 has now been canceled and the remaining claims renumbered. Enclosed herewith are replacement pages 35-37 replacing the corresponding pages of the application as filed.

PCT Article 33(3), Rejections

The Examiner has stated that claim 2 lacks an inventive step under PCT Article 33(3) as being obvious over Zemetra et al.

Claim 2 has now been canceled rendering moot the Examiners rejections with respect to this claim.

The Examiner also states that claims 3, 4 and 13 lack an inventive step under PCT Article 33(3) as being obvious over Zemetra et al. in view of Williams et al.

The Examiner points out that Zemetra et al. teach a method of preventing introgression of desirable traits from a genetically engineered crop species into a closely related weedy species, but do not teach control elements which are not functional in weeds.

Williams et al. teach the use of genetic engineering for pollination control and the use of inducible promoters for controlled expression of desired genes.

The Examiner concludes that it would have been obvious to one of ordinary skill in the art to utilize the method of Zemetra et al. along with the inducible promoters taught by Williams et al. given the recognition by those of ordinary skill in the art that choice of means to prevent gene transmission or expression in weeds would have been the optimization of process parameters.

Applicant respectfully submits that this statement is in error as the cited combination of references does not provide one skilled in the art with the basis or motivation to practice the presently claimed invention.

The claimed invention relates to genetic mechanisms for mitigating the effects of introgression of a genetically engineered genetic trait of a crop to a weed and of mitigating a weedy potential of the crop.

Claim 3 of the instant application relates to one possible mitigation method which is effected by introducing into a crop plant a control element inexpressible by the weed. Claims 4 and 13 relate to a construct utilizable by such method and a crop plant comprising such a construct, respectively.

As pointed out by the Examiner, Zemetra suggests mitigating introgression of a desirable trait by introducing the gene encoding such a desirable trait into a chromosome of a crop plant which would not introgress into a related weed.

In fact, Zemetra et al., suggests that the gene of choice be placed on a chromosome which, <u>in theory</u>, would not introgress into the weed; e.g., on the A or B genome of hexaploid wheat, and not on the D genome which is almost identical to the D genome of tetraploid *Aegilops cylindrica*.

In theory, such an approach would only work in two crop-weed pairs - wheat/Aegilops and oilseed rape (tetraploid AC) and *Brassica campestris* (C genome only).

Such mitigation of introgression approach would not be successful in crop-weed pairs which display close homology between respective genomes, such as, for example, rice-red rice and sunflowers-wild sunflowers.

In fact, numerous articles discuss the shortcomings of the method described by Zemera et al. To this end, see, for example, Tomiuk J, Hauser TP, Bagger-J˥rgensen R. 2000. A- or C-chromosomes, does it matter for the transfer of transgenes from *Brassica napus*. *Theoretical and Applied Genetics* 100: 750-4; Mikkelsen TR, Jensen J, Jorgensen RB. 1996. Inheritance of oilseed rape (*Brassica napus*) RAPD markers in a backcross progeny with *Brassica campestris*. *Theoretical and Applied Genetics* 92: 492-7 and Wang, ZN; Hang, A; Hansen, J; Burton, C; Mallory-Smith, CA; Zemetra, RS Visualization of A- and B-genome chromosomes in wheat (Triticum aestivum L.) x jointed goatgrass (Aegilops cylindrica Host) backcross progenies. GENOME, 43:1038-1044, 2000.

In sharp contrast, the claimed invention overcomes such a limitation by providing methods which do depend upon differences in genomic composition between crops and their respective weeds but rather takes advantage of variable gene expression and function. Thus, the methods of the claimed invention are not designed to prevent gene transfer but rather to prevent gene expression, function or alternatively to be detrimental to the weed when transferred.

In sharp contrast, the method described by Zemetra et al. attempts to block gene transfer, which as evident from the articles referenced above, is a near impossible task.

Williams et al. teach genetic engineering based methods of producing hybrid seeds in crop plants.

To produce such seeds, Williams et al. utilize construct systems for inducing male sterility which is reversible either through crossing or chemical induction of a counter-gene (inducible promoter recited on page 347, column 1, bottom paragraph).

Williams et al. do not teach nor do they suggest the use of such constructs or inducible promoters for mitigating introgression of a desired trait to a weed. In fact, it is possible that the chemically induced promoters described by Williams et al. are functional in weeds, since a crop restricted function of such inducible promoters is not described nor is it suggested by Williams et al.

Thus, since Zemetra et al., teaches chromosomal location of desired traits to prevent introgression and Williams et al. teach the use of inducible promoters for reversing male sterility, the cited references not only fail to provide teachings enabling or motivating one of skill in the art to practice the claimed invention, but also fail to provide any teachings that one skilled in the art would have a reasonable expectation of creating such methodology.

The Examiner further states that claim 1 lacks an inventive step under PCT Article 33(3) as being obvious over Zemetra et al. in view of Kultnow et al. further in view of Williams et al.

The Examiner states that although Zemetra et al. do not teach the use of apomictic male-sterile plants, Kultnow et al. teach the use of apomictic plants for the propagation of plants without pollination, while Williams et al. teach the use of genetic engineering to create male sterile plants for pollination control.

Thus, the Examiner points out that it would have been obvious to combine the teachings referenced above given the benefits of pollination control taught by each reference.

Applicant respectfully submits that this statement is in error. As detailed below, the cited combination of references does not provide one skilled in the art with the basis or motivation to practice the presently claimed invention.

Zemetra et al. and Williams et al. were discussed above. Kultnow et al. describe the process of apomictic development and the use of molecular approaches that may lead to the isolation of apomictic genes which can be used for the generation of genetically identical seeds without fertilization. As is clearly stated by Kultnow et al. throughout the document, apomictic genes and plants can be used for agricultural production of improved hybrid crops by maintaining hybrid vigor while avoiding the limitations inherent to other prior art methods utilized. Kultnow et al. do not describe nor do they suggest the use of apomixis in mitigating introgression between crop plants and related weeds.

Thus, both Williams et al. and Kultnow et al. describe methods applicable for hybrid seed technology, <u>and not for mitigating the effects of introgression</u>.

Contrary to plants generated by the methods proposed by Williams et al. and/or Kultnow et al., the male sterile, apomictic plants generated according to the method of claim 1 of the present invention would not impregnate weeds.

It is the Applicant's strong opinion that the approach of the present invention which combines male sterility with apomictic crop plants is not rendered obvious by the combined teachings of Zemetra et al., Williams et al. and Kultnow et al., since such methodology was not suggested by the teachings thereof and since the advantages of such combination cannot be inferred therefrom by one of ordinary skill in the art.

The Examiner also states that claims 5, 6, 9 and 13 lack an inventive step under PCT Article 33(3) as being obvious over Zemetra et al. in view of Paterson et al. and further in view of Young.

Paterson et al. teach that seed shattering is a trait important to weeds, identify the chromosomal location of the gene and also caution against the introgression of desirable traits from cultivated crop species into weedy species.

Young teaches the isolation of an anti-shattering gene.

The Examiner points out that it would have been obvious to one of ordinary skill in the art to utilize the method of Zemetra et al. and to modify it by incorporating the anti-shattering gene taught by Young as suggested by Paterson et al.

Applicant respectfully submits that this statement is in error. As detailed below, the cited combination of references does not provide one skilled in the art with the basis or motivation to practice the presently claimed invention.

Claims 5, 6, 9 and 13 of the present invention relate to methods of mitigating the effects of introgression of a genetically engineered first genetic trait of a crop to a weed and of mitigating a weedy potential of the crop, by co-engineering at least one copy of a genetically linked second genetic trait, encoding, for example, an anti-shattering function, in the crop which is innocuous or somewhat valuable to the crop yet deleterious to the weed.

In sharp contrast, Paterson et al. teach the use of a shattering gene for crop breeding. Although Paterson et al. "caution" against the use of transgenic sorghum, the use of shattering gene described thereby in an anti-shattering function (e.g., anti-sense) for the purpose of mitigating introgression is not described nor is it suggested.

Thus, It is the Applicant's strong opinion that an approach using an anti-shattering trait for mitigating introgression is not rendered obvious by the combined teachings of Zemetra et al., Paterson et al. and Young.

The Examiner also states that claims 5-7 and 11-13 lack an inventive step under PCT Article 33(3) as being obvious over Zemetra et al. in view of Paterson et al. and further in view of Snow et al.

Although Snow et al. analyses the ease with which crop to wild introgression can occur, and the fitness of the wild-crop hybrids and permeability of gene transfer. Snow et al. do not teach nor do they suggest methods useful for preventing such introgression.

As such, it is the Applicant's strong opinion that the combined teachings of Zemetra et al., Paterson et al. and Snow et al. do not render obvious claims 5-7 and 11-13 of the present invention.

The Examiner also states that claims 5, 6, 8 and 13 lack an inventive step under PCT Article 33(3) as being obvious over Zemetra et al. in view of Paterson et al. and further in view of Klee et al. (U.S. Pat. No. 5,512,466).

The Examiner points out that Klee et al. teach crop plant transformation with a gene which delays fruit ripening, which when combined with the teachings of Zemetra et al. and Paterson et al. renders obvious claims 5, 6, 8 and 13 of the present invention.

Applicant would like to point out in this respect that since Klee et al. do not describe nor do they suggest the use of such ripening genes and plants expressing same for mitigating introgression, the combined teachings of Zemetra et al. in view of Paterson et al. and further in view of Klee et al. do not render obvious claims 5, 6, 8 and 13 of the present invention.

The Examiner also states that claim 10 lacks an inventive step under PCT Article 33(3) as being obvious over Zemetra et al. in view of Paterson et al. and further in view of Schaller et al.

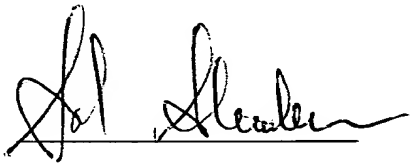
Again, Applicant would like to point out that since Schaller et al. do not describe nor do they suggest the use of dwarfism inducing genes and plants expressing same for mitigating introgression, the combined teachings of Zemetra et al. in view of Paterson et al. and further in view of Schaller et al. do not render obvious claims 5, 6, 8 and 13 of the present invention.

Therefore, contrary to the Examiner's assertion, the prior art cited does not add much to the teachings of Zemetra et al. to suggest the presently claimed invention and as such it fails to provide one of ordinary skill in the art with motivation to practice the various aspects of the claimed invention.

In conclusion, it is the Applicant's strong opinion that the prior art method of mitigating introgression described by Zemetra et al. does not render obvious the novel methods of mitigating introgression described and claimed by the instant application simply because the prior art method is combined with teachings of components utilizable by the methods of the present invention, especially in cases in which teachings or suggestion for use of such components in mitigating introgression are clearly lacking.

In view of the above remarks it is respectfully submitted that claims 1-12 are non-obvious with respect to the prior art cited. Favorable examination is hence respectfully and earnestly solicited.

Respectfully submitted,



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Date: January 28, 2001.